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Experimental studies on coronary perfusion with pump-oxygenator

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Abstract

1. Methods of retrograde coronary perfusion and direct coronary artery perfusion in combination with a bubble oxygenator were investigated in dogs. 2. Ventricular fibrillation occurred more frequently during the operation in hypothermia than in the operation performed in combination with the extracorporeal circulation. 3. The optimal pressure of perfusion is considered to be 30 to 35 mm Hg in retroperfusion, whereas, 100 mm Hg in direct coronary artery perfusion. 4. Perfusion by the pressure bottle method is preferable to the gravity method because the fall of blood temperature in the irrigation tubing might cause ventricular fibrillation. 5. From the metabolic study of the methods is clear that there is a tendency to myocardial anoxia after 15 to 20 minutes of perfusion in both methods.

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EXPERIMENTAL STUDIES ON CORONARY PERFUSION WITH PUMP-OXYGENATOR*

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Direct vision intracardiac surgery is nowadays a quite common procedure used in the most institutions in the world, although the open aortic valve surgery may still have serious obstacles to be encountered such as the myocardial hypoxia derived from the interruption of the coronary circulation and the coronary air embolism. In 1956, BLANCO and OKADA² have found a way of preventing the obstacle by perfusing the coronary vessels with oxygenated blood retrogradely through the coronary sinus in the open aortic valve operation. Thereafter, LILLEHEI³ succeeded in the clinical application of the method. However, in the retrograde coronary perfusion, though simple and feasible technically, the right ventricle hypoxia and myocardial ecchymosis were hardly avoidable.

In another paper⁴ we reported the method of the direct coronary artery perfusion with a brain cooling method in which the myocardium was nourished through the coronary artery ostia. However, it is well known that application of hypothermia frequently causes the ventricular fibrillation^{5,6,7,8,9,10} and the safe limit of the circulatory cessation is very short within which the operation must be finished. Consequently, the use of a pump-oxygenator is desirable for the operation at the normal body temperature. The first success of GIBBON¹¹ using a pump-oxygenator for the open heart surgery under direct vision, has been tested by many investigators. The clinical applications of this apparatus were first attempted by DENNIS¹¹ in 1951 and HNELMTHWORTH¹² in 1953, but both failed. In 1953 GIBBON¹³ again reported the first successful repair of an atrial septal defect utilizing entire cardiopulmonary by-pass with the pump-oxygenator designed by him.

Various apparatuses are now available to deliver pulsatile or continuous flows of the oxygenated blood by filming, bubbling, and dialysis. Among these methods, the bubble type of oxygenator devised by DEWALL¹⁴

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is most useful. In this paper, experiment on the coronary perfusion is studied in dogs by means of Model-III of Dewall type apparatus.

MATERIALS AND METHODS

For the extracorporeal circuit the pump consisting of a single electric motor and two metal finger pumps (Figs. 1, 2) which are regulated by separate transmissions is used. As the ventricle in the pumping chamber the Latex tubings, 14 mm in diameter, have been employed. The fingers were pre-set as to keep in "one point touch" with the pressure plates to avoid the mechanical destruction of red blood cells or the regurgitation. The oxygenator, depicted in Fig. 3, consists of an oxygen diffuser and a diffusing

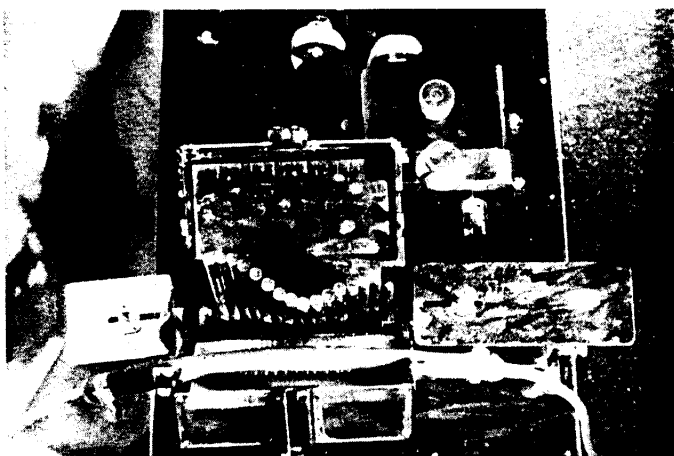


Fig. 1. The metal finger pump with its box opened and trasmission

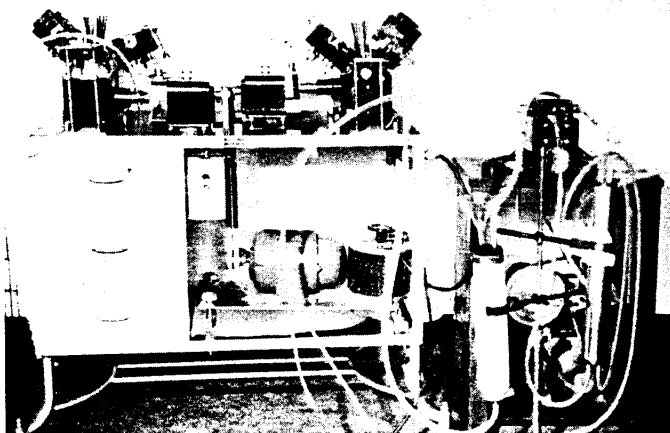


Fig. 2. A distant view of the pump unit and coronary sinus system

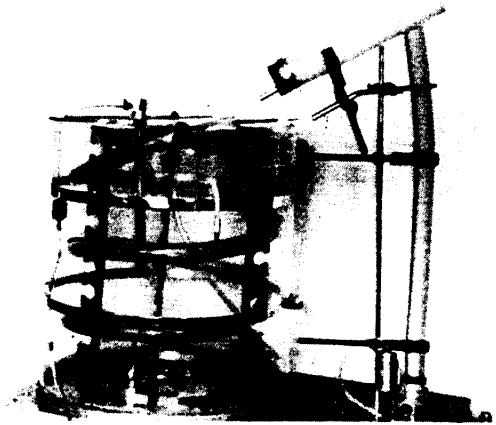


Fig. 3. Oxygen diffuser, vertical mixing tube, debubbling chamber and helix settling tube with nylon filter

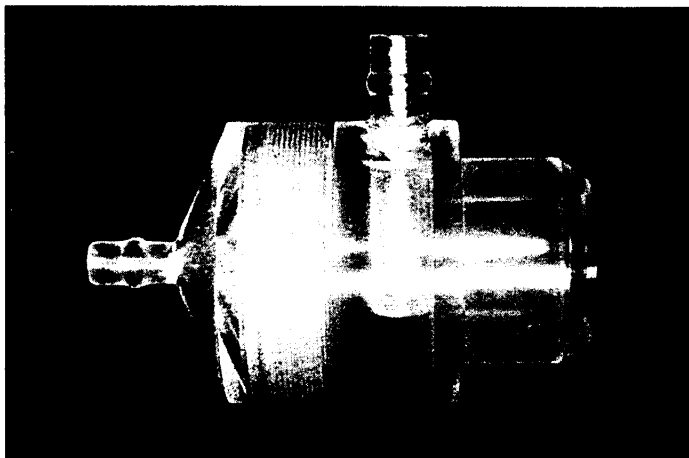


Fig. 4. Oxygen diffuser containing multiple perforated membrane

column (mixing tube set vertically). Oxygenation of the venous blood is accomplished by the direct introduction of 100 per cent of oxygen in the form of large bubbles into the mixing tube through the multiple perforations of the disc in the diffuser (Fig. 4). The top of the mixing tube is connected to a debubbling chamber with a capacity of 1,000 ml inside of which is coated with harmless silicon "Dow Corning Antifoam A" which eliminates large bubbles by momentary contact. Excess of oxygen and carbon dioxide is eliminated through the Ivalon sponge set at the end of the debubbling chamber. The oxygenated blood without bubbles passes into the Helix

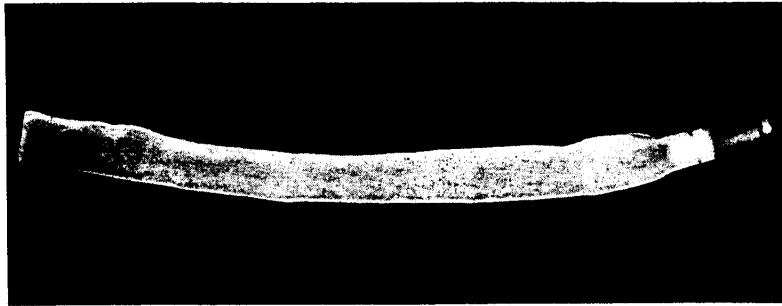


Fig. 5. Nylon filter with rubber stop which is set in the distal end of the helix settling tube by hose band.

settling tube with a capacity of 3,000 ml and is filtered through the fine nylon meshes (Fig. 5). The "Helix" is dipped in a water bath at 38 to 39°C and blood is pumped by the arterial pump-head to the dog. Venous blood was drained by gravity at 30 to 40 cm H₂O of pressure. An accessory sigma motor pump is employed to force back blood into the coronary sinus and Thebesian venous blood, which is forced to the venous side of the apparatus via a coronary sinus reservoir made of stainless steel, is oxygenated, and then recirculated.

Tubing used is of polyvinyl, two sorts in size, 10 mm and 8 mm in diameter. Connectors are of stainless steel with smooth tapered interior surface. Y-connectors are made of glass.

As the blood for circulation the blood was used adding 3 mg. Heparin, anticoagulant, per kg. of body weight.

Eight dogs ranging from eight to 15 kg. in weight were operated upon without any prospect of survival. Intravenous nembutal was used for anesthesia. Thoracotomy was performed through the anterior bilateral fourth intercostal incision transecting the sternum. Tapes were passed about the cavae to be tightened around the cannulae for complete inflow occlusion. The pericardium was incised anterior to the right phrenic nerve. After intravenous injection of Heparin three Mg. per kg. of body weight, superior vena cava was cannulated through the azygos vein, and inferior vena through the right auricular appendage. The arterial tract of the circuit was connected to the right femoral artery. Although some investigators regard blood aspirated from the open heart as "toxic" for its hemolysis, and frequently lethal when injected into the circulation intracardiac blood was recirculated through the "coronary sinus system" or correctly "intracardiac return system" in this series as reported by KIRKLIN¹⁵.

The rate of flow during complete heart lung by-pass was regulated

prior to the operation with the physiologic saline solution, in order that 60 cubic centimeters per kg. of body weight might be circulated through the pump. The problem of the flow rate is most difficult to be solved. WARDEN at first used three to 3.5 times of Azygos flow based upon the low flow principle¹⁶, though recently 45 to 65 cubic centimeters per kg. per minute are used¹⁷. COOLEY¹⁸ circulated for infants less than two years old 50 cubic centimeters per kg. of body weight and in patients over two years old 35 cubic centimeters per kg. of body weight. Oxygen flow through the diffusion plate was adjusted to be approximately ten times of the blood flow as COOLEY recommended¹⁸. The diagram of the circuit was illustrated in Fig. 6.

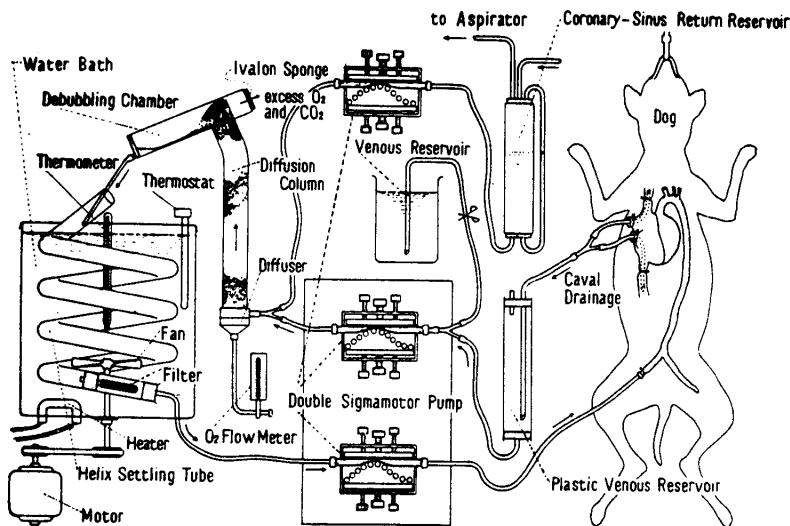


Fig. 6. Diagram illustrating the extracorporeal circuit using a bubble oxygenator of DeWall type.

a. Retrograde coronary perfusion with a pump-oxygenator :

After total inflow occlusion the right atrium was incised and the cannula was inserted into the coronary sinus. Coronary sinus flow during extracorporeal circulation was measured and the blood sample was taken as a control for metabolic study before the retroperfusion was started. Aorta was then cross clamped and incised longitudinally and retroperfusion of the coronary sinus was started. Three of the cases were perfused by gravity at 60 to 80 cm H₂O. While other five were irrigated with a pressure bottle at 30 to 100 mm Hg. During the retroperfusion blood was collected from the left coronary arteries through the fine catheters placed in the ostia and at the same time the flow was measured. The blood for coronary perfusion

was oxygenated and filtered by gauze sponge to remove fibrin mass and blood clot.

b. Direct coronary artery perfusion with a pump-oxygenator

From the observation in selective brain cooling by irrigation it has been elucidated that at least a few minutes were necessary for the cannulations into three coronary arteries during which coronary air embolism might occur and myocardial blood supply was interrupted. During this interval temporary retroperfusion has replaced the direct coronary artery perfusion. Twelve adult mongrel dogs were used in this series of experiments. Cross matching, anesthesia, and extracorporeal circulation were performed in the same way as described above. While blood supply to the myocardium maintained by the retroperfusion three polyethylene tubes were cannulated into the right coronary artery, the anterior descending artery and the left circumflex artery successively and fixed to the aortic wall to avoid dislodging. After finishing the cannulations, the myocardium was perfused in the physiologic direction (Fig. 11).

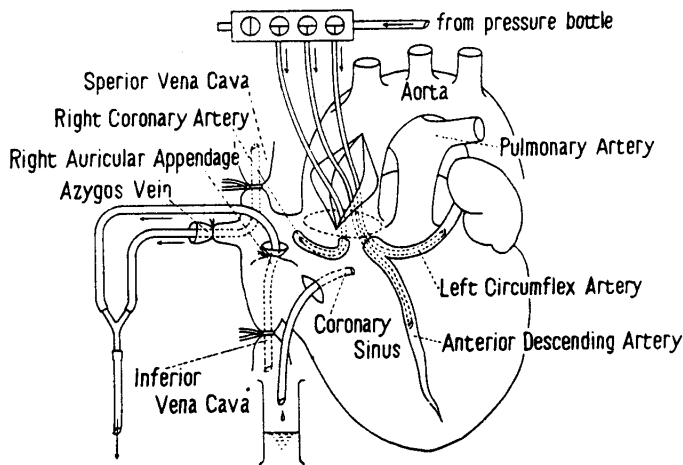


Fig. 11. Diagram of direct coronary artery perfusion utilizing a bubble oxygenator

RESULTS

a. Retrograde coronary perfusion :

The minimum flow rate of extracorporeal circulation in this series was 480 cubic centimeters per kg. of body weight per minute, and the maximum was 900 cubic centimeters per kg. of body weight per minute.

While the duration for total cardiopulmonary by-pass varied from 19 minutes 55 seconds to 53 minutes 59 seconds, the myocardium were perfused for 11 minutes 25 seconds up to 45 minutes 30 seconds.

Ventricular fibrillation occurred in four of eight cases studied, one of which could not be rescued by countershock and died. Heart beats were relatively good as compared to that in hypothermia. However, most of the cases showed cyanosis on the right ventricle surface after 15 to 20 minutes perfusion (Table 1). In two dogs which showed ventricular fibrillation (dogs 39, 45) there were found numerous filariae in the right ventricle and pulmonary artery at autopsy; in other two, on the contrary (dogs 40, 42), the perfused blood was too cold (about 31°C) which may have induced cardiac arrhythmia.

Table 1. Results of operation in retroperfusion utilizing a mechanical pump-oxygenator

Dog. No.	Wt. in Kg.	Perfusion Rate cc/min.	By-pass Time mins.	Perfusion Time mins.	Fibrillation	Mort.
37	14	840	51'59	45'30	(-)	Killed
39	14	840	50'00	47'00	Occurred	Killed
40	15	900	21'30	14'10	Occurred	Killed
41	13	780	41'00	36'20	(-)	Killed
42	13	780	31'30	26'30	Occurred	Killed
43	14	840	32'00	28'00	(-)	Killed
44	8	480	49'00	45'00	(-)	Killed
45	14	840	15'55	11'25	Occuried	Death

In three cases irrigated by gravity no myocardial bleeding appeared, but on the other hand, perfusion by the use of a pressure bottle at a pressure of 100 mm Hg caused the myocardial bleeding without exception, but not at a pressure below 35 mm Hg (Table 2).

Oxygen extraction in this series decreased gradually after perfusion as well as oxygen consumption (Fig. 7).

Table 2. Relationship between perfusion pressure and myocardial bleeding in retroperfusion

Dog No.	Perfusion Pressure mmHg	Myocardial Bleeding	Pressure bottle mmHg		
Gravity perfusion cmH ₂ O			41	100	(+)
			42	100	(+++)
37	80	(-)	43	35	(-)
39	60	(-)	44	30	(-)
40	80	(-)	45	30	(-)

Coronary Perfusion

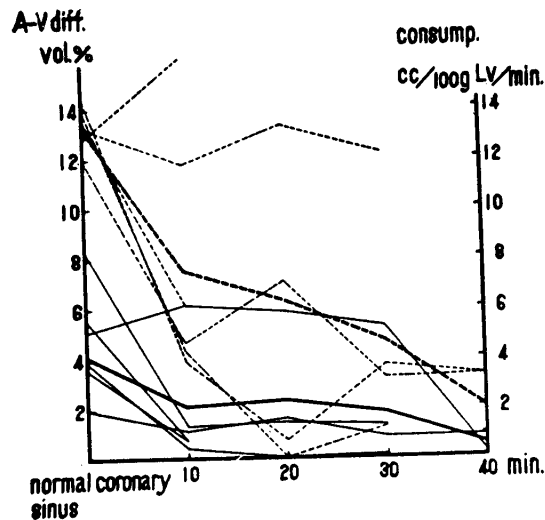


Fig. 7. Oxygen extraction and consumption in retroperfusion utilizing a bubble oxygenator. Light unbroken lines indicate consumption, and heavy unbroken line indicates the mean consumption. Light broken lines represent myocardial extraction, and heavy broken line represents the mean myocardial extraction. The explanation of the curves given above is common to all the figures.

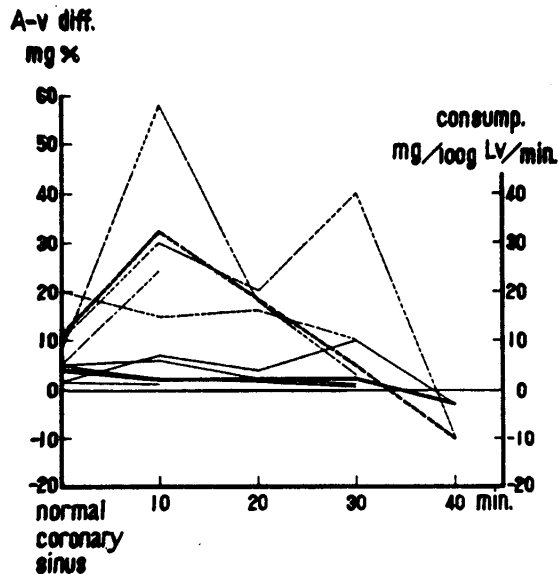


Fig. 8. Glucose metabolism in retroperfusion utilizing a bubble oxygenator

The glucose extraction shows a tendency to rise until 25 minutes after perfusion, and then decreased. The glucose consumption did not change significantly for 30 minutes and then decreased (Fig. 8).

Lactate metabolism showed negative extraction in two cases, but positive in one case where acetate extraction decreased after 25 minutes of perfusion and then inverted (Fig. 9). Consumption showed almost the same tendency.

Pyruvate reduced after 10 minutes perfusion, indicating myocardial anoxia (Fig. 10).

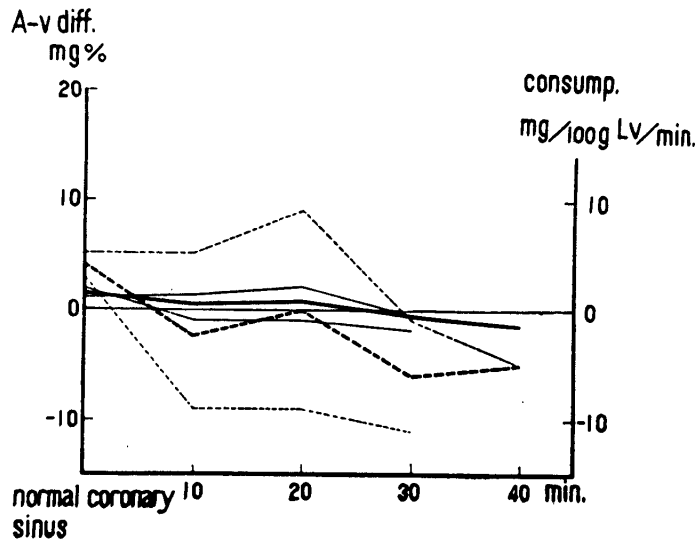


Fig. 9. Lactate metabolism in retroperfusion utilizing a bubble oxygenator

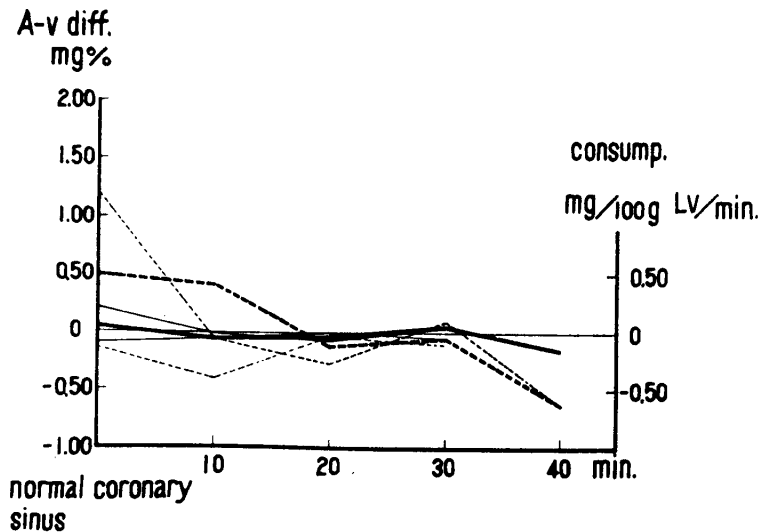


Fig. 10. Pyruvate metabolism in retroperfusion utilizing a bubble oxygenator

b. Direct coronary artery perfusion :

The rate of flow of the extracorporeal circulation ranged from 600 cubic centimeters up to 1,260 cubic centimeters per kg. of body weight per minute. On the other hand, by-pass period ranged from 13 minutes 33 seconds to 51 minutes. The duration of coronary perfusion was from 10 minutes 33 seconds to 48 minutes.

Ventricular fibrillation occurred in four of 12 cases (33.3%), three of which failed to be defibrillated by countershock. Fig. 12 shows the survey of incidence of ventricular fibrillation in our series of the experiments. From the figure it may be noticed that ventricular fibrillation occurs more frequently in the hypothermic state than in the by-passed heart and more frequently in the retroperfusion than in the direct coronary artery perfusion.

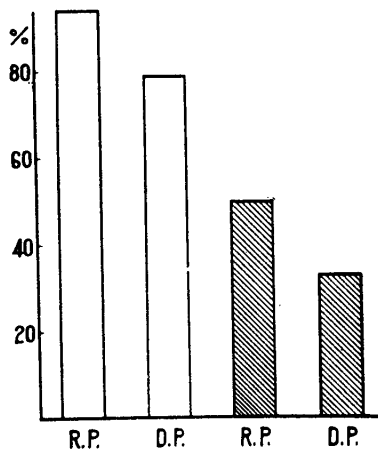


Fig. 12. Incidence of ventricular fibrillation

White column shows the incidence of V. F. in selective brain cooling. Striped column shows the incidence of V. F. in extracorporeal circulation.

R. P.: Retroperfusion, D. P.: Direct coronary artery perfusion.

Perfusion pressure of 90 to 120 mmHg or even 260 mmHg did not produce deleterious effect to the myocardium, though we reported in the previous paper¹⁹ that pressure over 60 mm Hg might cause the myocardial bleeding in the right ventricle (Table 4).

Oxygen extraction of the myocardium was slightly depressed during perfusion, especially after 20 minutes, while the oxygen consumption during the perfusion showed little change, though depressed to about 1/2 of the control before circulatory cessation (Fig. 13).

The glucose extraction showed a tendency to fall down after 20 minutes, as well as the myocardial glucose consumption (Fig. 14).

Lactate was consumed until 20 minutes of perfusion, then produced in the myocardium (Fig. 15).

Table 3. Results of operation in direct coronary artery perfusion utilizing a bubble oxygenator

Dog. No.	Wt. in Kg.	Perfusion Rate cc/min.	By-pass Time mins.	Perfusion Time mins.	Fibrillation	Mort.
46	10	600	51'00	48'00	(-)	Killed
47	17	1020	19'00	10'40	(-)	Killed
48	15	900	41'30	37'00	(-)	Killed
49	21	1260	13'33	10'33	Occurred	Death
50	10	600	39'20	34'00	(-)	Killed
51	14	840	33'50	29'25	(-)	Killed
52	15	900	33'10	26'45	(-)	Killed
53	17	1020	30'00	17'08	(-)	Killed
54	16	960	27'48	22'38	(+)	Doath
55	12	720	27'00	13'00	(+)	Death
56	14	840	32'17	27'59	(+)	Deatb
57	12	720	28'00	25'30	(-)	Death

Table 4. Relationship between perfusion pressure and myocardial bleeding in direct coronary perfusion

Dog No.	Perfusion Pressure Pressure Bottle mmHg.	Myocardial Bleeding			
46	100 to 120	(-)	52	120	(-)
47	100	(-)	53	100	(-)
48	100	(-)	54	260	(-)
50	100	(-)	65	100	(-)
51	90 to 100	(-)	56	100	(-)
			57	100	(-)

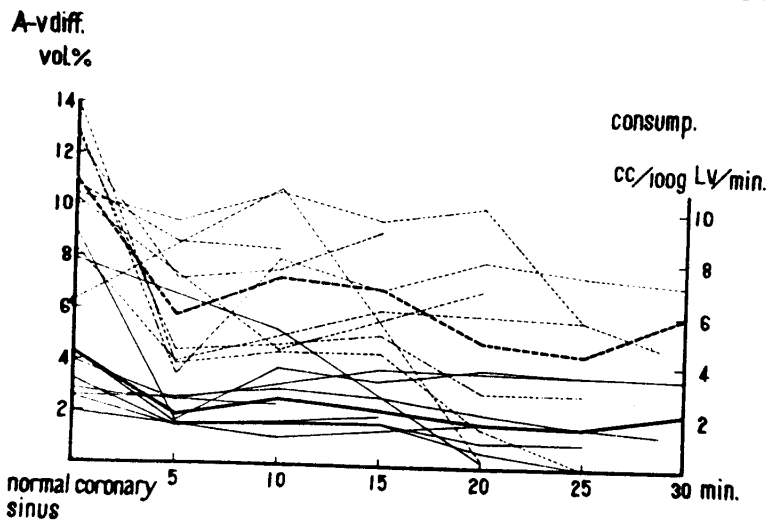


Fig. 13. Oxygen extraction and consumption in direct coronary artery perfusion utilizing a bubble oxygenator

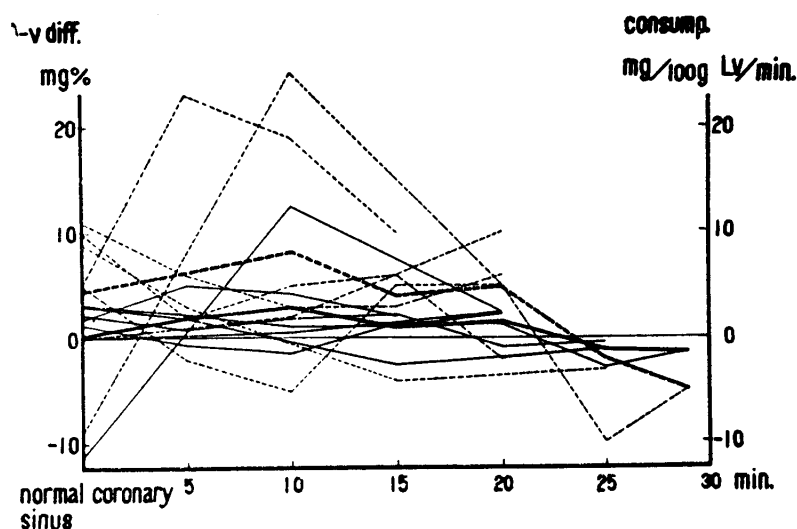


Fig. 14. Glucose metabolism in direct coronary artery perfusion utilizing a bubble oxygenator

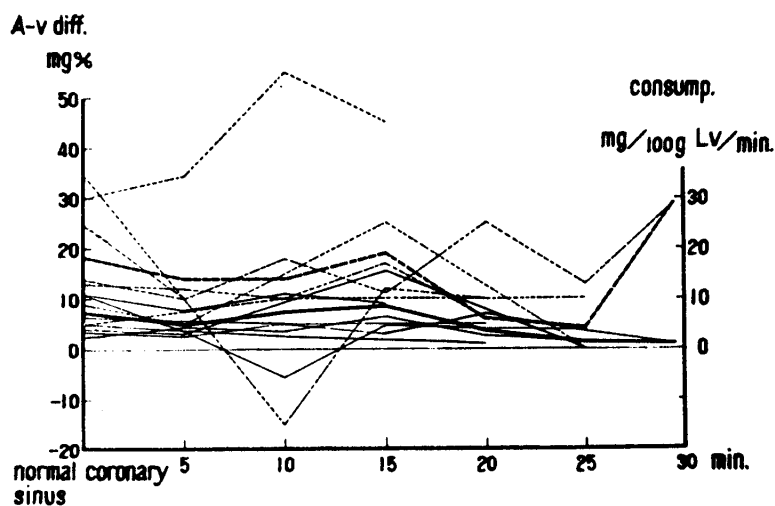


Fig. 15. Lactate metabolism in direct coronary artery perfusion utilizing a bubble oxygenator.

Pyruvate extraction and consumption via the myocardium showed a steep fall after 15 minutes of perfusion (Fig. 16).

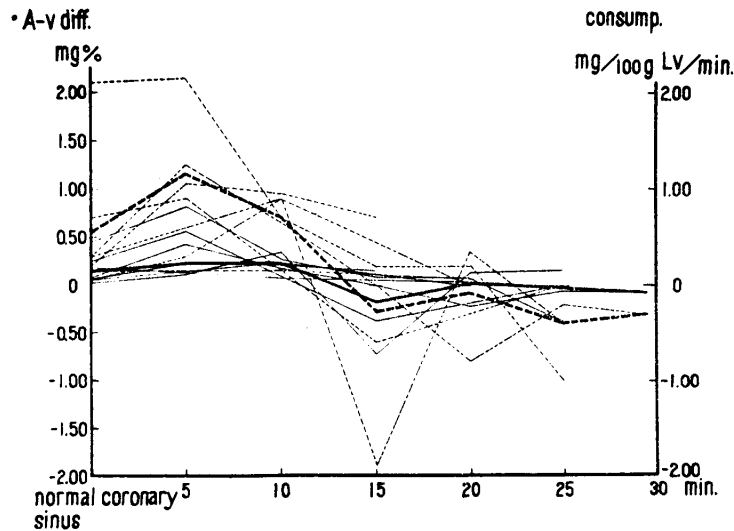


Fig. 16. Pyruvate metabolism in direct coronary artery perfusion utilizing a bubble oxygenator

DISCUSSION

Application of coronary perfusion with the aid of selective brain cooling by irrigation to the aortic valve surgery was somewhat disappointing for its high incidence of ventricular fibrillations. However, the introduction of bubble oxygenator in combination with coronary perfusion encouraged us to perform this type of the operation. The contraction of the heart are apparently forcible in this method as compared with that in hypothermia.

As pyruvate production in the myocardium is an important indicator of myocardial ischemia²⁰, so lactate elimination is caused by deficit in oxygen supply²¹. From the above experiments, it appears that the myocardium shows a tendency to anoxic state in both methods.

Although the retroperfusion has various undesirable features as above mentioned, this method is considered to be feasible and safe if it is performed in combination with a mechanical pump-oxygenator and the time of coronary sinus perfusion is limited within 15 to 20 minutes. On the contrary, direct coronary artery perfusion is thought to allow longer periods of safe circulatory cessation in the open reparative surgery of aortic valve or ascending aorta. A tendency to myocardial anoxia in direct coronary artery perfusion may be derived from insecure cannulation, dislodging during perfusion, and local insufficient blood supply due to wedging

of the cannula, which would be improved in the human case.

Electrolyte changes were not measured in this experiment because of hemolysis occurring in the course of extracorporeal circulation¹¹, and of recirculation of normal saline solution aspirated from the thoracic cavity during the operation.

SUMMARY AND CONCLUSION

1. Methods of retrograde coronary perfusion and direct coronary artery perfusion in combination with a bubble oxygenator were investigated in dogs.

2. Ventricular fibrillation occurred more frequently during the operation in hypothermia than in the operation performed in combination with the extracorporeal circulation.

3. The optimal pressure of perfusion is considered to be 30 to 35 mm Hg in retroperfusion, whereas, 100 mm Hg in direct coronary artery perfusion.

4. Perfusion by the pressure bottle method is preferable to the gravity method because the fall of blood temperature in the irrigation tubing might cause ventricular fibrillation.

5. From the metabolic study of the methods is clear that there is a tendency to myocardial anoxia after 15 to 20 minutes of perfusion in both methods.

ACKNOWLEDGEMENT

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